21/28'CL. Amino acid residues are numbered using the convention of Kabat et al. The underlined numbers indicate the specificity determining residues (SDRs). CDR1, CDR2 and CDR3 within the light chain of HuCC49 and CC49 correspond to SEQ ID NOs: 1-3, respectively. CDR1, CDR2 and CDR3 within the heavy chain of HuCC49 and CC49 correspond to SEQ ID NOs: 4-6, respectively. CDR1, CDR2 and CDR3 within the light chain of human antibody LEN correspond to SEQ ID NOs: 7-9, respectively. CDR1, CDR2 and CDR3 within the heavy chain of human antibody 21/28'CL correspond to SEQ ID NOs: 10-12, respectively.

Please replace the paragraph at page 6, lines 22-26 with the following:

Figure 11 shows the amino acid sequences of V_L frameworks of human MAb LEN (SEQ ID NOS: 33-36) and humanized V_L of CC49 (HuCC49) (SEQ ID NO: 13) in panel A. Panel B shows the amino acid sequences of V_H frameworks of human MAb 21/28'CL (SEQ ID NOS: 37-40) and humanized V_H of CC49 (HuCC49) (SEQ ID NO: 14). Framework residues that are deemed to be important in maintaining the combining site structure of CC49 are marked by an asterisk.

Please replace the paragraph at page 6, lines 27-32 with the following:

Figure 12 shows the nucleotide sequence of HuCC49 variable light (V_L) region (SEQ ID NO: 41 and SEQ ID NO: 42) and variable heavy (V_H) region (SEQ ID NO: 43 and SEQ ID NO: 44) genes in panels A and B, respectively. Sequences of flanking oligomers that do not encode the variable region domains or their leader peptides are shown in lowercase letters. The V_L region (A) is encoded by nucleotides from positions 74 to 412, while nucleotides from position 70 to 415 (B) comprise the V_H region. The four overlapping oligomers depicted by long arrows in Figure 12A are represented by SEQ ID NOs: 19-22. The four overlapping oligomers depicted by long arrows in Figure 12B are represented by SEQ ID NOs: 15-18.

Please insert the following text at page 7, line 29, immediately preceding the section entitled "Definitions":

Sequence Listing

The nucleic and amino acid sequences listed in the accompanying sequence listing are shown using standard letter abbreviations for nucleotide bases and three letter code for amino acids, as defined in 37 C.F.R. 1.822. In the accompanying sequence listing:

SEQ ID NO: 1 shows the amino acid sequence of CDR1 from the light chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 2 shows the amino acid sequence of CDR2 from the light chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 3 shows the amino acid sequence of CDR3 from the light chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 4 shows the amino acid sequence of CDR1 from the heavy chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 5 shows the amino acid sequence of CDR2 from the heavy chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 6 shows the amino acid sequence of CDR3 from the heavy chain of murine antibody CC49 and humanized antibody HuCC49.

SEQ ID NO: 7 shows the amino acid sequence of CDR1 from the light chain of human antibody LEN

SEQ ID NO: 8 shows the amino acid sequence of CDR2 from the light chain of human antibody LEN

SEQ ID NO: 9 shows the amino acid sequence of CDR3 from the light chain of human antibody LEN

SEQ ID NO: 10 shows the amino acid sequence of CDR1 from the heavy chain of human antibody 21/28'CL

SEQ ID NO: 11 shows the amino acid sequence of CDR2 from the heavy chain of human antibody 21/28'CL

SEQ ID NO: 12 shows the amino acid sequence of CDR3 from the heavy chain of human antibody 21/28'CL

SEQ ID NO: 13 shows amino acids sequence of the V_L domain of the humanized murine antibody HuCC49.

SEQ ID NO: 14 shows amino acids sequence of the V_H domain of the humanized murine antibody HuCC49.

SEQ ID NOs: 15-32 show several synthetic oligonucleotides useful as probes and/or primers.

SEQ ID NOs: 33-36 show amino acid sequences of consecutive portions of the framework of the V_L domain of the human antibody LEN.

SEQ ID NOs: 37-40 shows amino acid sequences of consecutive portions of the framework of the V_H domain of the human antibody 21/28'CL.

SEQ ID NO: 41 show the nucleic acid sequence including the V_L domain of the humanized murine antibody HuCC49 together with flanking oligomers.

SEQ ID NO: 42 shows the nucleic acid sequence complementary to SEQ ID NO: 41.

SEQ ID NO: 43 shows the nucleic acid sequence including the V_H domain of the humanized murine antibody HuCC49 together with flanking oligomers.

SEQ ID NO: 44 shows the nucleic acid sequence complementary to SEQ ID NO: 43.

Please replace the paragraph at page 19, lines 3-12 with the following:

According to the invention, CDR variants are formed by replacing at least one CDR of CC49 in HuCC49 with a corresponding CDR from a human antibody. The CDR variants of the invention include:

- Variant L-1: L-CDR1 of CC49 (SEQ ID NO: 1) was replaced with L-CDR1 of LEN (SEQ ID NO: 7).
- Variant L-2: L-CDR2 of CC49 (SEQ ID NO: 2) was replaced with L-CDR2 of LEN (SEQ ID NO: 8).
- Variant L-3: L-CDR3 of CC49 (SEQ ID NO: 3) was replaced with L-CDR3 of LEN (SEQ ID NO: 9).
- Variant L-1,2: L-CDR1 and L-CDR2 of CC49 (SEQ ID NOs: 1 and 2, respectively) were replaced with L-CDR1 and L-CDR2 of LEN (SEQ ID NOs: 7 and 8, respectively).
- Variant H-1: H-CDR1 of CC49 (SEQ ID NO: 4) was replaced with H-CDR1 of 21/28'CL (SEQ ID NO: 10).

- Variant H-2: H-CDR2 of CC49 (SEQ ID NO: 5) was replaced with H-CDR2 of 21/28'CL (SEQ ID NO: 11).

Variant H-3: H-CDR3 of CC49 (SEQ ID NO: 6) was replaced with H-CDR3 of 21/28'CL (SEQ ID NO: 12).

Please replace the paragraph at page 19, lines 15-28 with the following:

Synthesis of three variant V_H genes was performed using the overlap extension PCR technique described by Kashmiri et al., (1995) Hybridoma 14:461-473. Four 123-126 base pair long overlapping oligonucleotides (SEQ ID NOs: 15-18) (which together encompass the entire sequence of the variant V_H gene on alternating strands) were used to generate variant V_H genes. (Figure 12 B) The oligomers were supplied by Midland Certified Reagent Co., Midland, TX. Instead of a template DNA, the PCR mixture contained 2 pmoles of the four oligonucleotides. PCR was carried out by three cycles of a denaturing step at 94°C for 1 minute, a primer annealing step at 55 °C for 2 minutes, and an extension step at 70°C for 2 minutes, followed by 17 additional cycles of denaturation (94°C, 1 minute), primer annealing (55°C, 2 minutes), and extension (72°C, 1 minute). All polymerase chain reactions (PCRs) were carried out in a final volume of 100 Tl of PCR buffer containing 100 TM of dNTPs, 5 units of Taq DNA polymerase (Boehringer Mannheim) and 20 pmol of each end primer.

Please replace the paragraph at page 19, lines 31-35, and page 20, lines 1-17, with the following:

The three variant V_L genes were generated using 30-43 base oligonucleotides as a mutagenic primer. The oligonucleotides contained the desired base changes in the targeted CDR. The mutagenic primers for the V_L genes were synthesized using a Model 8700 DNA synthesizer (Miligen/Bioresearch, Burlington, VT). (Figure 12 A) Primer induced mutagenesis was carried out by a two-step PCR method, as described by Landt et al., (1990) Gene, 96:125-128. pLNXCHuCC49HuK (Kashmiri et al, (1995) Hybridoma 14:461-473) (Figure 2) was used as a template in both steps. In the first step, the mutagenic primer was used as a 3' primer while a 20 nucleotide long end primer served as a 5' primer. The product of the first PCR was gel purified and utilized as a 5' primer for the second PCR in which a 20 nucleotide long end primer was used as a 3' primer. The 20 nucleotide long end primers used for DNA amplification were

supplied by Midland Certified Reagent Co. (Midland, TX). The sequences for these primers are reported by Kashmiri et al., (1995) Hybridoma 14:461-473 and are as follows:

1. 5' V_H, 5'-CTA AGC TTC CAC CAT GGA G-3' (SEQ ID NO: 23)
2. 3' V_H, 5'-ATG GGC CCG TAG TTT GGC G-3' (SEQ ID NO: 24)
3. 5' V_L, 5'-GCA AGC TTC CAC CAT GGA TA-3' (SEQ ID NO: 25)
4. 3' V_L, 5'-AGC CGC GGC CCG TTT CAG TT-3' (SEQ ID NO: 26)

Each of the primers carries a single restriction endonuclease site at its flank. The 5' primers carry a *Hind*III site, while the 3' V_H primer carries an *Apa*I, and the 3' V_L primer has a *Sac*II site. The restriction endonuclease recognition sequences are underlined.

Please replace the paragraph at page 30, lines 22-27, and page 31, lines 1-15, with the following:

Mutagenic oligonucleotide primers, ranging in size from 37 to 56 nucleotides, were synthesized using a Model 8700 DNA synthesizer (Milligen/Bioresearch, Burlington, VT). They were purified on oligo-Pak columns (Milligen/Bioresearch) according to the supplier's recommendation. The sequences of the mutagenic primers were as follows, where the mutagenic changes are underlined:

V_L CDR3:

5'-GCC AGC GCC GAA GCT GAG GGG ATA GCT ATA ATA CTG CTG ACA-3' (SEQ ID NO: 27)

5'-GGT GCC AGC GCC GAA GCT GAG GGG GGT GCT ATA ATA CTG CTG ACA-3' (SEQ ID NO: 28)

5'-GCC ACG GCC GAA TGT GTA GGG ATA GCT ATA ATA CTG CTG ACA -3' (SEQ ID NO: 29)

5'-GCC GAA TGT GAG GGG GGT GCT ATA ATA CTG CTG ACA ATA-3' (SEQ ID NO: 30)

V_H CDR1:

5'-GTT TCA CCC AGT GCA TTG CAT AAT CAG TGA AGG TGT A-3' (SEQ ID NO: 31)

V_H CDR2:

5'-GTG GCC TTG CCC TGG AAC TTC TGT GAG TAC TTA AAA TCA TCG TTT CCG GGA GAG AA-3' (SEQ ID NO: 32)

Please replace the sequence listing as follows:

Please enter the enclosed replacement sequence listing to replace the existing sequence listing in the subject application.

In the Drawings:

Please replace page 2/23 of the drawings as originally filed with attached substitute page 2/23.